JAN - 2 2014

510(k) Summary

This summary of 510(k) safety and effectiveness information is submitted in accordance with the requirements of SMDA 1990 and 21 CFR §807.92.

The assigned 510(k) number is: K133512

1. Manufacturer's Name, Address, Telephone, and Contact Person, Date of Preparation

Manufacturer:	Siemens Healthcare Diagnostics Inc. P.O. Box 6101 Newark, DE 19714
Contact Information:	Siemens Healthcare Diagnostics Inc. P.O. Box 6101 Newark, DE 19714 Attn: A. Kathleen Ennis Regulatory Affairs Manager Tel: 302-631-9352 FAX # 302-631-6299
Date of Preparation:	December 30, 2013

2. Device Name

Proprietary Name

- LOCI Vitamin B12 Flex® reagent cartridge
- LOCI Anemia Calibrator

Common Name

- Vitamin B12 Assay
- Calibrator

FDA Classification

- Radioassay Vitamin B12 - code CDD
- Calibrator Multianalyte - code JIX

3. Identification of the Predicate Device

- Dimension Vista® Vitamin B12 Flex® reagent cartridge (VB12) k121994
- Dimension Vista® LOCI 4 CAL k121994

FDA Guidance Document(s):

- "Bundling Multiple Devices or Multiple Indications in a Single Submission"-11/26/2003

4. Device Description(s):

LOCI VB12 Assay

The vitamin B12 method is a homogeneous, competitive chemiluminescent immunoassay based on LOCI® technology. LOCI® reagents include two synthetic bead reagents and biotinylated intrinsic factor (IF). The first bead reagent (Chemibead) is coated with a B12 derivative and contains a chemiluminescent dye. The second bead reagent (Sensibead) is coated with streptavidin and contains photosensitive dye. The patient sample is pretreated with sodium hydroxide (NaOH) and dithioerythritol (DTE) to release the serum B12 from its carrier proteins. Potassium cyanide (KCN) is added to convert all the forms of B12 into a single, cyanocobalamin form, and dicyanocobinamide is added to keep the B12 from rebinding with the carrier proteins. After the sample pretreatment, the biotinylated IF and chemibead reagents are added sequentially to the reaction vessel. Vitamin B12 from the sample competes with the B12-chemibead for a limited amount of biotinylated IF. Sensibead reagent is then added and binds to the biotin to form bead pair immunocomplexes. Illumination of the complex at 680 nm generates singlet oxygen from the Sensibeads which diffuses to the Chemibeads triggering a chemiluminescent reaction. The resulting signal is measured at 612 nm and is an inverse function of the concentration of vitamin B12 in the sample.

The LOCI VB12 method reagents are packaged in an eight-well Flex® reagent cartridge as follows:

Wells[a]	Form	Ingredient	Concentration[b]	Source
1	Liquid	VB12 Sensibead reagent	360 µg/mL	Recombinant *E. coli*
2	Liquid	VB12-Chemibead reagent	200 µg/mL	
3	empty			
4	Liquid	Biotinylated IF Dicyanocobinimide	3 ng/mL 60 ng/mL	porcine
5	Tablet	Dithioerythritol (DTE)	12.5 mg/mL	
6	Liquid	Sodium Hydroxide (NaOH) Potassium Cyanide (KCN)	0.75 N 3 mM	
7-8	empty			

a. Wells are numbered consecutively from the wide end of the cartridge.
b. Nominal value per well in a cartridge.

Each cartridge contains a sufficient to perform 20 tests. Four (4) Flex® reagent cartridges are provided in each carton.

LOCI Anemia Calibrator

LOCI ANEMIA CAL is a multi-analyte liquid, frozen product containing Folate and Vitamin B12. All levels are prepared in a bovine serum albumin base.

The kit consists of ten vials, two each of five levels containing 2 mL per vial. Description of the manufacturing, value assignment and stability testing processes are provided.

Values are assigned to each lot of calibrator from a master pool using the Dimension® EXL with LM integrated chemistry system. The master pool is a frozen liquid, five level material, with the same composition as the calibrator with traceability to USP Grade Vitamin B12.

The assigned to LOCI Anemia Calibrator are stable for unopened frozen product until the expiration date on the label. Unopened (Thawed) product is stable for 30 days when stored at 2-8°C. Once the product is opened (cap removed), assigned values are stable for 30 days when recapped immediately after use and stored at 2-8°C. Shelf life and in use stability have been established by Siemens Healthcare through real time testing at the temperatures specified,

5. Device Intended Use:

LOCI VB12 Assay
The VB12 method is an *in vitro* diagnostic test for the quantitative measurement of Vitamin B12 (B12) in human serum and plasma on the Dimension® EXL™ with LM integrated chemistry system. Measurements of Vitamin B12 may be used in the diagnosis of vitamin B12 deficiency.

LOCI Anemia Calibrator
The LOCI ANEMIA CAL is an *in vitro* diagnostic product for the calibration of the LOCI FOLA and LOCI VB12 assays on the Dimension® EXL™ with LM integrated chemistry system.

6. Medical device to which equivalence is claimed:

Substantial Equivalence:
The LOCI Vitamin B12 Flex® reagent cartridge (RF642) is substantially equivalent to the Dimension Vista® Vitamin B12 method (k#121994). The LOCI Anemia Calibrator (RC640) is substantially equivalent to the LOCI 4 Calibrator, cat.# KC640A (k#121994).

Comparison to Predicate Device:
The proposed Siemens Healthcare Diagnostics LOCI VB12 method and the predicate Dimension Vista® VB12 method (k121994) are both *in vitro* diagnostic immunoassays intended for the quantitative measurement of vitamin B12 in serum and plasma.

The Siemens Healthcare Diagnostics LOCI Anemia Calibrator, cat. # RC640 and the predicate Siemens LOCI 4 Calibrator, cat. # KC640A (K121994) are both used for the calibration of Folate and Vitamin B12 methods.
A comparison summary of the features of the products is included in the following table.

LOCI VB12 Assay:

Item	Device LOCI Vitamin B12 Flex® reagent cartridge	Predicate Dimension Vista® Vitamin B12 Flex® reagent cartridge (k121994)
Similarities		
Intended Use	*in vitro* diagnostic test for the quantitative measurement of vitamin B12 in human serum and plasma	*in vitro* diagnostic test for the quantitative measurement of vitamin B12 in human serum and plasma
Sample Types	Serum and Plasma	Serum and Plasma
Measurement method	Chemiluminescent: Homogenous sandwich immunoassay based on LOCI® technology	Chemiluminescent: Homogenous sandwich immunoassay based on LOCI® technology
Sample Size	12 uL	12 uL
Differences		
Instrument	The Dimension® EXL™ with LM System	The Dimension Vista® System.
Measuring Range	80 – 2000 pg/mL	60 – 2000 pg/mL

LOCI Anemia Calibrator:

Item	Device LOCI Anemia Calibrator (ANEM CAL)	Predicate LOCI 4 Calibrator (k121994)
Similarities		
Intended Use	The LOCI ANEM CAL is an *in vitro* diagnostic product for the calibration of the LOCI FOLA and LOCI VB12 assays on the Dimension® EXL™ with LM System.	The LOCI 4 CAL is an *in vitro* diagnostic product for the calibration of the LOCI Ferritin (FERR), LOCI Folate (FOL) and LOCI Vitamin B12 (VB12) methods on the Dimension Vista® System.
Traceability		
Folate	United States Pharmacopeia Grade Folic Acid	United States Pharmacopeia Grade Folic Acid
Vitamin B12	United States Pharmacopeia Grade vitamin B12	United States Pharmacopeia Grade vitamin B12
Form	Frozen Liquid	Frozen Liquid
Target Concentrations VB12	Level 1 : 45 pg/mL Level 2 200 pg/mL Level 3 500 pg/mL Level 4 1000 pg/mL Level 5: 2200 pg/mL	Level A: 45 pg/mL Level B: 200 pg/mL Level C: 500 pg/mL Level D: 1000 pg/mL Level E: 2200 pg/mL
Folate	Level 1: 0 ng/mL Level 2: 2.5 ng/mL Level 3: 5.0 ng/mL Level 4: 10.0 ng/mL Level 5: 21.0 ng/mL	Level A: 0 ng/mL Level B: 2.5 ng/mL Level C: 5.0 ng/mL Level D: 10.0 ng/mL Level E: 21.0 ng/mL
Differences		
Matrix	bovine serum albumin base in levels 1 - 5	HEPES buffer Level A
		bovine serum base (BSA) in levels B - E
Constituents	LOCI ANEM CAL is assigned for vitamin B12 and Folate.	LOCI 4 CAL is assigned for vitamin B12, Folate and Ferritin

Comments on Substantial Equivalence:

Method

The Siemens Healthcare Diagnostics Dimension® LOCI VB12 method and the predicate Siemens Healthcare Diagnostics Dimension Vista® LOCI VB12 method (k121994) are both *in vitro* diagnostic immunoassays intended for the measurement of vitamin B12 in serum and plasma.

Reproducibility testing was conducted for the Dimension® LOCI VB12 method in accordance with the CLSI/NCCLS Approved Guideline for User Evaluation of Precision Performance of Clinical Chemistry Devices EP5-A2. For each test level, a single test from two independent cups was analyzed twice per day for 20 days. The repeatability and within-lab standard deviations were calculated by the analysis of variance method.

Typical precision observed for the Dimension® LOCI VB12 method is summarized below:

Material	Mean pg/mL	Repeatability		Within-Lab Precision	
		SD	%CV	SD	%CV
Bio-Rad Liquichek® Immunoassay Control*					
L1	290	13.2	4.6	15.0	5.2
L2	498	11.7	2.3	18.2	3.7
L3	645	15.9	2.5	21.5	3.3
Serum Pool 1	180	10.1	5.6	11.6	6.5
Li Heparin Plasma Pool	467	13.1	2.8	15.8	3.4
Serum Pool 2	978	24.9	2.5	27.7	2.8
Serum Pool 3	1733	27.4	1.6	35.2	2.0

*BioRad Liquichek™ Immunoassay Plus Controls, BioRad Laboratories, Irvine, CA

A total of seventy-eight (78) matched serum, lithium heparin plasma, sodium heparin and EDTA plasma samples were analyzed on the Dimension ® EXL™ System. Of these 71 were native samples, 6 were spiked and one was diluted. Each plasma type was analyzed versus serum. Serum Separator tubes (SST) were analyzed in the same study. The Passing-Bablok regression analysis was used to analyze the data. The results are as follows:

Sample Type (vs Serum) n = 78	Slope	95% Confidence Interval	Intercept pg/mL	95% Confidence Interval pg/mL
Lithium Heparin Plasma	1.00	0.99 – 1.02	-4.33	-13.4 to +2.5
Sodium Heparin Plasma	1.02	0.99 – 1.04	-10.73	-20.2 to -0.4
EDTA Plasma	1.00	0.98 – 1.02	-7.26	-15.8 to +3.5
SST Tubes	1.01	0.99 – 1.03	-2.31	12.0 to + 6.3

A method comparison between the LOCI VB12 assay on the Dimension® EXL™ with LM System and the predicate, Dimension Vista® VB12 method (k121994), was performed with 166 native human serum samples across the proposed assay range. The samples ranged from 60 - 1966 pg/mL with the Dimension Vista® VB12 method, and, 86 - 1901pg/mL with the LOCI® VB12 assay on the Dimension® EXL™ with LM integrated chemistry system. These samples included thirty-five (35) samples that were positive for Intrinsic Factor Blocking Antibody (IFBA) with titers ranging from 15 - 164 IU/mL.

Passing-Bablok regression analysis of the results yielded the following:

Passing & Bablok Regression			
	Bias	95% CI	
Intercept(pg/mL)	-6.37	-12.90	to 0.36
Slope	1.03	1.02	to 1.04

The correlation coefficient, using least squares regression, for this data set (r) is 0.997.

Conclusion:

The Siemens Healthcare Diagnostics LOCI VB12 method and the predicate Siemens Healthcare Diagnostics Dimension Vista® VB12 method (k121994) are substantially equivalent based on their intended use and performance characteristics as described above. The calibrator products, the Siemens Healthcare Diagnostics LOCI Anemia Calibrator and the predicate Dimension Vista® LOCI 4 Calibrator (K121994) are also substantially equivalent in its design and intended use with their respective assay systems.

Anna Marie K. Ennis
Regulatory Affairs Manager
December 30 2013

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

January 2, 2014

SIEMENS HEALTHCARE DIAGNOSTICS
ANNA MARIE KATHLEEN ENNIS
P.O. Box 6101
500 GBC DRIVE M/S 514
NEWARK DE 19714-6101

Re: K133512
Trade/Device Name: LOCI Vitamin B12 Flex® Reagent Cartridge and LOCI Anemia Calibrator
Regulation Number: 21 CFR 862.1810
Regulation Name: Vitamin B12 test system
Regulatory Class: II
Product Code: CDD, JIX
Dated: November 5, 2013
Received: November 15, 2013

Dear Ms. Ennis:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the

electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Carol C. Benson -S for

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): k133512

Device Name: LOCI vitamin B12 Flex® Reagent Cartridge and LOCI Anemia Calibrator

Indications for Use:

The VB12 method is an in vitro diagnostic test for the quantitative measurement of Vitamin B12 (B12) in human serum and plasma on the Dimension® EXL™ with LM integrated chemistry system. Measurements of Vitamin B12 may be used in the diagnosis of vitamin B12 deficiency.

The LOCI ANEMIA CAL is an in vitro diagnostic product for the calibration of the LOCI FOLA and LOCI VB12 assays on the Dimension® EXL™ with LM integrated chemistry system.

Prescription Use __X___ (21 CFR Part 801 Subpart D) And/Or Over the Counter Use ____. (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostics and Radiological Health (OIR)

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Division Sign-Off
Office of In Vitro Diagnostics and Radiological Health

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